REMARKS

Status of the Claims

Claims 1-14, and 21-26 are currently pending in the application. Claims 1, 21 and 22 are amended. New claims 24-26 are added.

Support for amendment

The amendment to claims 1 and 21 is supported by the specification at page 7, Example 1. This amendment corrects a mistake of calculation made in amending the claims in the previous amendment.

The amendment to claim 22 deletes an inadvertently included phrase.

New claims 24-26 are supported by the specification at least at page 6, in the third line of the last paragraph.

Rejection under 25 USC § 112, first paragraph

Claims 1, 2, 5, 6, 8, 9, 11-14, 22 and 23 are rejected under 35 USC § 112, first paragraph for lack of written description support in the specification. In particular, the Examiner asserts that in claims 1 and 21 the specification does not provide description of the feature of the claims that up to 75% of the claimed composition is DMSO and up to 25% of the claimed composition is cyclosporin. Applicants acknowledge their miscalculation of proportion as pointed out by the Examiner and have corrected claims 1 and 21 accordingly, thus obviating this basis for rejection.

The Examiner also asserts that the specification does not support the recitation in claim 22 that the amount of cyclosporin provided is from 0.001 mg/kg body weight/day to 1000 mg/day. As pointed out in Applicant's previous Amendment, these endpoints are described at page 6, in the last paragraph. See line 5 for the lower endpoint and line 3 for the upper endpoint. While it is true that the lower endpoint is for one route of administration and the upper endpoint relates to a different route of administration, both are clearly contemplated in the specification at the time the application was filed. Accordingly, the rejection based on the failure of the specification to describe these endpoints should be withdrawn.

Rejections under 35 USC § 103(a)

Claims 1-14 and 21-23 stand rejected under 35 USC § 103(a) as being unpatentable over Kaswan '047 in view of Elzinga (1989), Broadwell (1982) and Elias '820. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested, as the Examiner fails to establish *prima facie* obviousness of the claimed invention.

The Examiner admits that Kaswan '047 **FAILS TO** disclose or suggest the following features of the claims:

a) methods for administering a cyclosporin and DMSO solution by injection into the cerebrospinal fluid, intra-ocular, intravestibular, into or adjacent to the brain or spinal cord, or intravenous, intra-arterial, intraparenchymal spaces, or orally, rectally, vaginally, urethrally, bladder cisternally, nasally, intra- and peri-ocularly or dermally to a patient,

b) an article of manufacture comprising packaging material and a pharmaceutical agent wherein said agent comprises DMSO and a cyclosporin formulation,

c) a method for treating Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, HIV neuropathy, Guillain-Barré syndrome, neural transplantation, neural xenotransplantation, stroke, brain hemorrhage, brain and spine trauma, ionizing radiation, neurotoxicity of vestibular structures, or retinal detachment (claim 11), and

d) a method for inducing systemic immunosuppression in patients of transplantation or autoimmune disease (claim 12).

To this list, Applicant would add that the very high proportion of DMSO recited in claims 1, 21 and claims dependent thereon is not disclosed or suggested by the combination of references cited.

The Examiner's position is essentially that the additional references somehow establish *prima facie* obviousness of the invention as presently claimed because they teach that 1) DMSO is an effective solvent for carrying a compound across the blood-brain barrier and 2) that administration of DMSO to a subject in an amount of less that 15% of a composition and in a total amount of 0.25 to 0.5 ml did not exhibit any hemorrhage.

First of all, with respect especially to claim 3, the mode of administration is one in which the blood-brain barrier is irrelevant. There is no barrier to transport of a compound to central nervous system tissues from the compartments of the body that are filled with cerebrospinal fluid. Furthermore, **none of the references cited by the Examiner contemplate introduction of ANY composition into the cerebrospinal compartments of a subject.** At least the method of claim 3 is patentable over the cited references.

Second, an absorption rate of 4 to 26% is not the same thing as a formulation proportion of from 0.1 to 25% (of cyclosporin). The Elzinga reference, so far as relied upon by the Examiner, is thus completely irrelevant to the present invention. Furthermore, the Examiner is completely ignoring the very high proportion of DMSO indicated in the present claims 1 and 21 and claims dependent thereon.

Third, as Applicant has explained previously, the Broadwell reference in fact discloses that, at high concentrations, DMSO has toxic effect when administered by injection in large amounts. Applicant directs the Examiner again to the explanations presented at page 10 of the Amendment of April 10, 2006.

Elias also fails to remedy the deficiencies of the Examiner's allegation of *prima facie* obviousness. The text of col. 9, lines 36-37 indicates a composition including only 24% DMSO (30% of 80%). This is far below the 80% DMSO indicated in the present claims 1 and 21 and claims dependent thereon.

The Applicant submits that the Examiner has completely failed to properly establish *prima facie* obviousness of the invention as presently claimed. The Examiner's arguments show a blatant disregard for recitations in the claims underlies his assertion of obviousness. The Examiner is requested to reconsider his position **and to take into account ALL of the recitations of the present claims**. Applicant submits that, upon such reconsideration, the instant rejection should be withdrawn for the reasons set forth above.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $225.00 is attached hereto.

If the Examiner has any questions or comments, Mark J. Nuell, Ph.D. at 858-792-8855.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 
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